

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
19 October 2000 (19.10.2000)

PCT

(10) International Publication Number
WO 00/61549 A3

- (51) International Patent Classification⁷: C07C 327/34, 69/618, 69/65, C07D 207/16, C07C 211/49, 219/10, C07D 209/28, 233/64, 277/06, 277/14, 295/088, 309/30, 401/12, 407/04, 417/12, 473/08, 495/04, 499/32, C07F 9/38, C07H 15/252, A61K 31/16
- (21) International Application Number: PCT/EP00/03237
- (22) International Filing Date: 11 April 2000 (11.04.2000)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
MI99A000750 13 April 1999 (13.04.1999) IT
- (74) Agents: SAMA, Daniele et al.; Sama Patents, Via G.B. Morgagni 2, I-20129 Milano (IT).
- (81) Designated States (*national*): AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, DM, EE, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- Published:
— with international search report
- (71) Applicant (*for all designated States except US*): NICOX S.A. [FR/FR]; 45, Avenue Kléber, F-75116 Paris (FR).
- (88) Date of publication of the international search report:
3 January 2002
- (72) Inventor; and
- (75) Inventor/Applicant (*for US only*): DEL SOLDATO, Piero [IT/IT]; Via Toti, 22, I-20052 Monza (IT).
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*



WO 00/61549 A3

(54) Title: PHARMACEUTICAL COMPOUNDS

(57) Abstract: Compounds or their salts of general formula (I): A-(B) wherein A = R-T₁-, wherein R is the drug radical and T₁ = (CO)_t, or (X)_{t'}, wherein X = O, S, NR_{1C}, R_{1C} is H or an alkyl having from 1 to 5 carbon atoms, or a free valence, t and t' are integers and equal to zero or 1, with the proviso that t = 1 when t' = 0; t = 0 when t' = 1; B = -T_B-X₂ wherein T_B = (CO) when t = 0, T_B = X when t' = -, X being as above defined; X₂, monovalent radical, is such that the precursor drug of A and the precursor of B respectively meet the pharmacological tests described in the application.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 00/03237

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07C327/34 C07C69/618 C07C69/65 C07D207/16 C07C211/49
C07C219/10 C07D209/28 C07D233/64 C07D277/06 C07D277/14
C07D295/088 C07D309/30 C07D401/12 C07D407/04 C07D417/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07C C07D C07H A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BEILSTEIN Data, WPI Data, EPO-Internal, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 052 910 A (ALBERTO REINER & C.) 2 June 1982 (1982-06-02) the whole document	1,3, 9-11, 16-18
X	EP 0 255 164 A (ZAMBON) 3 February 1988 (1988-02-03) the whole document	1,3, 9-11,16, 18



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

9 April 2001

Date of mailing of the international search report

08/05/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

English, R

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 00/03237

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D473/08 C07D495/04 C07D499/32 C07F9/38 C07H15/252
A61K31/16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHEMICAL ABSTRACTS, vol. 107, no. 7, 17 August 1987 (1987-08-17) Columbus, Ohio, US; abstract no. 59488w, page 781; XP002164473 abstract - & ES 8 609 231 A (FARMHISPANIA) 16 December 1986 (1986-12-16)	1,3, 9-11, 16-18
X	EP 0 103 320 A (EDMOND PHARMA) 21 March 1984 (1984-03-21) example 3	1,3, 9-11,16, 18
A	WO 98 47534 A (KLINGE PHARMA) 29 October 1998 (1998-10-29) page 12 -page 13	16-18

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the International filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

9 April 2001

Date of mailing of the international search report

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

English, R

FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

Continuation of Box I.2

Claims Nos.: 1-11,15-18 (not searched in part), 12-15 (not searched)

Present claims 1-18 relate to an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

Furthermore, present claims 1-18 relate to compounds defined by reference to a desirable characteristic or property, namely that their precursors attain a certain level of anti-oxidative activity evidenced according to test 4 and test 5 (which are elucidated in claim 1) and at least a certain level of at least one of (a) gastrointestinal damage, (b) apoptosis or (c) hepatic damage and/or gastric damage and/or cardiovascular damage evidenced according to tests 1 to 3 (also elucidated in claim 1). Since the combination these properties (anti-oxidative activity and lower toxicity) is in fact the problem to be solved by the compounds of the present application (see page 9, lines 1-11 of the description), this means that the claimed compounds are defined in terms of their being a solution to this problem.

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds prepared in examples 1-28.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Publication No

PCT/EP 00/03237

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0052910 A	02-06-1982	IT 1134458 B CH 648297 A DE 3169890 D JP 1028744 B JP 1543778 C JP 57167963 A	13-08-1986 15-03-1985 15-05-1985 05-06-1989 15-02-1990 16-10-1982
EP 0255164 A	03-02-1988	IT 1213301 B AT 96150 T AT 179071 T DE 3752272 D DE 3752272 T DE 3787844 D DE 3787844 T EP 0565146 A ES 2060592 T ES 2133351 T GR 3030822 T JP 63023857 A US 4806567 A US 4812477 A	20-12-1989 15-11-1993 15-05-1999 27-05-1999 30-12-1999 25-11-1993 10-02-1994 13-10-1993 01-12-1994 16-09-1999 30-11-1999 01-02-1988 21-02-1989 14-03-1989
ES 8609231 A	16-12-1986	ES 549540 D	01-09-1986
EP 0103320 A	21-03-1984	IT 1190987 B AT 27270 T BE 897617 A CA 1202317 A DE 3371627 D FR 2532647 A US 4563443 A	24-02-1988 15-06-1987 16-12-1983 25-03-1986 25-06-1987 09-03-1984 07-01-1986
WO 9847534 A	29-10-1998	AU 2387997 A EP 0971743 A	13-11-1998 19-01-2000